

REMARKS

Applicant respectfully requests reconsideration. Claims 1, 3, 4, 6, 7, 9-16 and 20-37 were previously pending in this application. By this amendment, Applicant is amending claims 1, 4, 7, and 9 to exclude colon cancer. No claims have been cancelled. New claims 38-43 have been added. Support for the new claims can be found in the claims as filed. As a result, claims 1, 3, 4, 6, 7, 9-16 and 20-43 are pending for examination with claims 1, 4, 7, 38, 40, and 42 being independent claims. No new matter has been added.

Rejections under 35 U.S.C. § 102

Claims 1, 3, 4, 6, 7, 9-16, 20-37 are rejected under 35 U.S.C. § 102(e) as being anticipated by Berger et al. (US Patent Application Publication No. 2003/0148410 A1).

Without conceding the correctness of the rejection and solely in an effort to expedite prosecution, Applicant has amended claims 1, 4, 7 and 9 to exclude colon cancer. As currently amended, the claims are not anticipated by Berger et al.

Rejections under 35 U.S.C. § 103

Claims 1, 3, 4, 6, 7, 9-16, 20-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5):1489-501, May 1999), and further in view of Berger et al. (U.S. Patent Application Number 2003/0148410 A1). The Office Action maintains the rejection that it would have been *prima facie* obvious for one of ordinary skill in the art to combine the teachings of Iba et al. and Berger et al. to arrive at the instant claims.

Applicant respectfully disagrees and requests reconsideration of this rejection. One of ordinary skill in the art would not have substituted the tumor tissue samples taught by Iba et al. with the biological fluids taught by Berger et al. because the results of the substitution would not have been predictable. Applicant respectfully maintains that the teachings found within the references themselves would not have led the skilled artisan to the combination. The combination would only have been effected using hindsight reasoning as discussed below.

The Supreme Court stated in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), 82 USPQ2d 1385 (2007), "rejections on obviousness cannot be sustained by mere conclusory

statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious, and an explicit analysis in supporting such a rejection (emphasis added).

MPEP §2143 lists several examples of rationales that may be used to establish a *prima facie* case of obviousness (i.e., combining prior art elements according to known methods to yield predictable results, simple substitution of one known element for another to obtain predictable results, etc.). Applicant acknowledges and appreciates that the exemplary rationales provided in MPEP §2143 are not all-inclusive, and that other rationales may be relied upon to support an obviousness rejection.

As a preliminary matter, Applicant respectfully notes that the Office Action fails to explicitly indicate any of the rationales set forth in MPEP §2143 in support of its claim rejections. The Office Action fails to specify whether it is relying on one of the rationales from this list, or adopting a different rationale; accordingly, Applicant has been left to speculate as to the rationale underlying the rejections. In view of the foregoing, Applicant has endeavored in good faith to map the rejections set forth in the Office Action to one of the rationales set forth in MPEP §2143 so as to provide an exemplary construct for demonstrating the impropriety of the rejections, as well as the patentability of all claims over the cited references. To this end, again while not clear from the Office Action itself, the Office Action appears to rely on the second rationale, “(B) simple substitution of one known element for another to obtain predictable results,” in support of the assertion that Applicant’s independent claims are purportedly rendered obvious by Iba et al. and Berger et al.

MPEP §2143(B) describes in detail the requirements for rejecting a claim based on this rationale. This section of the MPEP states that the Office Action must articulate the following:

- (1) a finding that the prior art contained a device (method, product, etc.) which differed from the claimed device by the substitution of some components (step, element, etc.) with other components;
- (2) a finding that the substituted components and their functions were known in the art;

(3) a finding that one of ordinary skill in the art could have substituted one known element for another, and the results of the substitution would have been predictable.

MPEP § 2143(B) further notes that “[t]he rationale to support a conclusion that the claim would have been obvious is that the substitution of one known element for another yields predictable results to one of ordinary skill in the art.”

The Office Action has failed to establish a *prima facie* case of obviousness, as the required findings set forth in MPEP §2143(B) are not met. In particular, the Office Action fails to establish that one of ordinary skill in the art could have substituted one known element for another, and that the results of such a substitution would have been predictable.

More specifically, the cited references provide no teaching or motivation for one of ordinary skill in the art to combine the references in the manner suggested by the Examiner. Based on the teachings of Iba et al. a person of ordinary skill in the art would not have substituted the tumor tissue samples described in Iba et al. with the biological fluids as taught in Berger et al. Moreover, the substitution of tumor tissue samples as taught by Iba et al. with the biological fluids of Berger et al. would not have yielded a predictable result. Applicant respectfully asserts that, based on the teachings of Iba et al., a skilled artisan would expect that any method directed to the detection and characterization of cancer would require measuring the levels of the membrane-bound ADAM 12-L in the tissue as the secreted form of the protein ADAM 12-S is present in both normal and tumor tissue.

MPEP §2141.02(VI) sets forth that “a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention (emphasis original). MPEP §2143.01(II) further states that “where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another.”

Iba et al. teaches that ADAMs are a family of membrane-bound cell surface proteins with a putative role in cell-cell and/or cell-matrix interactions (Page 1489). Furthermore, Iba et al. teaches that “in addition to the expected membrane-anchored form, designated ADAM 12-L, an alternatively spliced, secreted form exists, designated ADAM 12-S” (Page 1490, first column).

However, when the expression of both forms of ADAM 12 were measured, it was found that ADAM 12-S (the secreted form of the protein) was present in both normal and tumor tissue. ADAM 12-L (the membrane-anchored form), on the other hand, was present at higher levels in breast carcinoma than normal breast tissue (see page 1493, second column). Thus, according to Iba et al. the membrane-anchored form ADAM 12-L was up-regulated and not the secreted form ADAM 12-S. In light of these teachings, a skilled artisan would have no expectation that ADAM 12-S can be used in any method directed to the detection and characterization of cancer. To ignore this teaching of Iba et al. and substitute urine and blood fluids requires hindsight involving the teachings of the instant invention.

The Office Action contends that since the claims do not delineate any particular form of the protein, Applicant's arguments addressing particular forms of ADAM 12 are moot. Applicant respectfully disagrees and submits that the instant claims should not be restricted to any particular form of the protein. Based on the teachings of Iba et al. a person of skill in the art would not have a reason or a motivation, let alone have a reasonable expectation of success, to measure the expression levels of ADAM 12-S in a biological sample for the detection and/or prognosis of cancer because ADAM 12-S is present in both normal and tumor tissue. Furthermore, because ADAM 12-L is membrane-bound, a skilled artist would not have any expectation of success in detecting ADAM 12-L in the biological samples of the instant claims. Thus, according to prior art, neither form of ADAM 12 can be used in a method directed to the detection and characterization of cancer using urine and blood fluid samples. The teachings found within the cited references themselves would not have led the skilled artisan to the combination.

Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

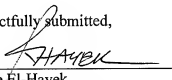
A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1285.70006US01 from which the undersigned is authorized to draw.

Dated: November 13, 2009

Respectfully submitted,

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